

OBITUARY

Matthew H Kaufman FRSE (1942–2013)

We are sad to report the early death of Matthew Kaufman, emeritus Professor of Anatomy at the University of Edinburgh and the leading mouse developmental anatomist of his generation. In a long and very productive research career, he wrote more than 200 papers and a dozen books on mouse development and on Scottish medical history.

Matt grew up in a very orthodox and rather poor Jewish family in London. His parents saw him as a future scribe, writing the Torah (the five books of Moses) in Hebrew on parchment, but the only long-term effect of this was his exquisite handwriting. His own life choice was to study medicine at the University of Edinburgh, where after qualification he specialized in obstetrics. This led him to become interested in reproductive physiology and to work as a research associate with Professor Anne McLaren at her Edinburgh MRC research unit. Realising that he much preferred research to medical practice, he moved to the Marshall Laboratory in the Department of Physiology, University of Cambridge in 1970 to study for a PhD on mouse parthenogenesis under the supervision of Professor C. R. (Bunny) Austin. After this, he spent two years at the Weizmann Institute in Israel with Professor Leo Sachs, returning to Cambridge as a University Demonstrator then University Lecturer in anatomy. His early work was summarized in a monograph, *Parthenogenetic Studies* (1983, C.U.P.).

Matt's first major contribution to science was to collaborate with Martin Evans in the development of mouse embryonic stem (ES) cells – these were initially called Evans-Kaufman (EK) cells. The five papers they published together

in 1981–4, together with those of Gail Martin in the USA at around the same time, provided the baseline knowledge for all subsequent work on the genetic manipulation of ES cells, their use in making transgenic mouse strains and their potential in regenerative medicine. Matt's contribution to this work was mainly the dissection of blastocysts to provide inner cell mass cells for culture, using the fine manipulative skills he had acquired during his parthenogenesis studies. Although he took no part in the exploitation of the technique for genetic manipulation, it was his knowledge of the use to which ES cells were being put that led to his recognition of the need for a resource of information on mouse developmental anatomy. It is the production of this resource for which he is now best known: his *Atlas of Mouse Development*, was a huge labour of love that took a decade to complete. For it, Matt analyzed, photographed and provided detailed labels and explanations for around 1500 micrographs of sections from all 26 Theiler stages of mouse embryos, together with diagrams and scanning electron micrographs of each stage. The sections of older stages include over 100 labels for each. The timing of its publication in 1992 was perfect, coinciding as it did with an explosion of studies on the developmental expression of newly cloned genes in mouse embryos, when molecular biologists new to embryology desperately needed an accessible source of information for the interpretation of new in situ hybridization patterns. By the standards of books on mouse development, this book has been and continues to be a bestseller (to the pleasant surprise of Academic Press, the publisher); a multi-author supplement that will be part of Matt's legacy is in preparation. It will include a set of coronal sections (few of which were included in the original book) that he prepared and partly labeled before his death.

In addition to its originally intended function, the *Atlas* provided the anatomical infrastructure used to compile the informatics of mouse development currently in use for the formal storage of new data on normal and abnormal mouse genetics. Around the time of publication, mouse informatics was getting off the ground both at the Jackson Laboratory in Maine and at the MRC Human Genetics Unit in Edinburgh, and it was soon clear that more was needed than just the basic genomics. One of us (JBLB) approached Matt and suggested that, for each Theiler stage, we should integrate all of the tissues into a "parts-of" hierarchy. One benefit of this would be that his beloved *Atlas* would get a proper index; another of course would be that the hierarchy (which soon became an ontology) could be used as the anatomical core for a database to which could be added tissue-associated data (e.g. gene-expression). This was

implemented by the Jackson Laboratory and is now a key feature of the mouse informatics resource there. The collaboration also resulted in a book with JBLB, *The Anatomical Basis of Mouse Development*, which links the *Atlas* to the development of the various organ systems. At the MRC Human Genetics Unit, Richard Baldock, Duncan Davidson and JBLB decided to go further and to make 3D reconstructions of mouse embryos from the slides that Matt had used for his *Atlas* and to include all the tissue boundaries so that gene expression could be shown accurately. This led Baldock and Davidson to produce the first online graphical atlas for capturing gene-expression data, to which Matt continued to provide detailed anatomical input until about 2011.

In 1985, some years earlier, Matt had been appointed to the chair of anatomy at the University of Edinburgh, a post established in 1705; he remained there until his retirement in 2007. The University did not view his tenure of the chair as entirely successful for two reasons. First, they had hoped that he would introduce molecular biology into the department, but he was not really equipped to do this. Second, they wished to reduce the amount of anatomical teaching in the curriculum to make room for genetics and social medicine; this shocked Matt because he believed that all of medicine stemmed from anatomy and that the best way of teaching anatomy, as well as the rest of medicine, was from the cadaver. He therefore opposed the inevitable changes at every stage. In hindsight, he lost more battles than he need have done, probably because for all his academic strengths his personality did not equip him to be a successful university politician. The problems were exacerbated by ill health: in 1995 he developed polycythaemia, a myeloproliferative neoplasm resulting in the overproduction of red blood cells. He spent the rest of his life on the maximum dose of

methotrexate that his body could tolerate, and lived in a state of continuous discomfort.

This is not to say that he had stopped or, indeed, ever stopped his involvement in research and scholarship. He had a deep love of anatomy, both mouse and human, and served on the editorial board of *Journal of Anatomy* for many years as an advisor and referee for embryological research articles. His interest in the medical history (mainly of anatomy) of Scotland in general and the University of Edinburgh in particular led him to write a series of articles and books on medical history from 1992 onwards. The most important of these was a history of the Edinburgh chair of anatomy that was part of the exhibition he organized in 2005 to celebrate the 300th anniversary of its foundation. By this time he was approaching retirement and there was some degree of reconciliation between him and the University. Indeed, there was no argument when, in 2007, he was elected to the Royal Society of Edinburgh.

Matt was fortunate in having a very happy home life. Claire, his wonderfully tolerant wife, put up with his never-ending work, his 1930s Lagonda car that was always breaking down and the sheer quantity of working papers, historical documents, research publications and histological slides that littered the house as well as his very large office in the university. Matt was a loving husband and father; Claire and their two sons are justly proud of him. We, his friends and former colleagues in Cambridge (GMMK) and Edinburgh (JBLB), join them in remembering with affection his somewhat eccentric interests, his kindness, his ability, his old-fashioned courtesy and his personal warmth.

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